



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

October 5, 2016

MEMORANDUM

SUBJECT: Formation of the Chemical Assessment Advisory Committee (CAAC)
Augmented for the Review of the EPA's Draft IRIS Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) Toxicological Review

FROM: Diana Wong, Ph. D. /s/
Designated Federal Officer (DFO)
EPA Science Advisory Board Staff Office (1400R)

THRU: Wanda Bright /s/
Ethics Officer
EPA Science Advisory Board Staff Office (1400R)

TO: Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

The National Center for Environmental Assessment (NCEA) in the EPA's Office of Research and Development (ORD) develops toxicological reviews/health assessments for various chemicals for EPA's Integrated Risk Information System (IRIS). NCEA developed a draft IRIS toxicological review of Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) and has released an external review draft in September 2016. NCEA has asked the Science Advisory Board (SAB) to peer review the 2016 draft toxicological review for RDX.

This memorandum addresses the set of determinations that were used in augmenting the CAAC for the RDX Review including:

1. The type of review body that will be used to conduct the review, and the nature of the review;
2. The types of expertise needed to address the general charge;
3. Financial conflict of interest considerations, including identification of parties who are potentially interested in or may be affected by the topic to be reviewed;
4. How regulations concerning "appearance of a loss of impartiality" pursuant to 5 C.F.R.

§ 2635.502 apply to members of the augmented committee;

5. Other considerations that might affect the objectivity of members of the augmented committee; and
6. How individuals were selected for the augmented committee.

DETERMINATIONS:

1. The type of review body that will be used to conduct the review, and the nature of this review.

The Chemical Assessment Advisory Committee (CAAC), a standing committee of the SAB, will be augmented by subject matter experts to conduct a peer review of EPA's *Toxicological Review of Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)* (External Review Draft - September 2016). The CAAC Augmented for the RDX Review will provide independent advice to the EPA Administrator through the chartered SAB.

2. The types of expertise needed to address the general charge.

On March 18, 2016, the EPA SAB Staff Office announced in a Federal Register Notice (Volume 81, Number 53, Pages 14849-14850) that it was augmenting the CAAC with additional experts to review and provide independent expert advice through the Chartered SAB on the EPA's *Toxicological Review of Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)* (External Review Draft - September 2016). To augment the CAAC, the SAB Staff Office sought public nomination of nationally and internationally recognized scientists in one or more of the following areas, with a particular focus on RDX: neurotoxicity; kidney/urogenital expertise [preferably with some experience with the prostate], reproductive/developmental toxicity, general toxicology; carcinogenicity; physiologically-based pharmacokinetic (PBPK) modeling including toxicokinetic considerations; and quantitative risk assessment expertise specifically related to dose-response modeling of animal data.

3. Financial conflict of interest consideration, including identification of parties who are potentially interested in or may be affected by the topic reviewed.
 - (a) Identification of parties (or class of parties) whose financial interests may be affected by the matter to be reviewed: The principal interested and affected parties as a class for this topic are organizations or industry sectors that may be affected by policies or regulations developed on the basis of EPA's *Toxicological Review of Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)*. RDX is not produced commercially in the United States (ATSDR, 2012). Current production in the United States is limited to Holston Army Ammunition Plant in Kingsport, Tennessee for use in military munitions (ATSDR, 2012). In the past, several Army ammunition plants may have also handled and packaged RDX. In 1980, RDX was produced at five commercial chemical production facilities in the United States (ATSDR, 2012). Since the manufacturers or users of RDX are limited in number and represent discrete and identifiable class of people or specific parties, the work to be done by the augmented committee meets the criteria for

a particular matter involving specific parties.

- (b) Conflict of interest considerations: For Financial Conflict of Interest (COI) issues, the basic 18 U.S.C. § 208 provision states that: “An employee is prohibited from participating *personally or substantially* in an official capacity in any *particular matter* in which he, to his knowledge, or any person whose interests are imputed to him under this statute has a *financial interest*, if the particular matter will have a *direct and predictable effect* on that interest [emphasis added].” For a conflict of interest to be present, all elements in the above provision must be present. If an element is missing the issue does not involve a financial conflict of interest; however, the general provisions in the appearance of impartiality guidelines still apply and need to be considered.
- (i) Does the general charge to the Augmented CAAC for RDX involve a particular matter? A “particular matter” refers to matters that “...will involve deliberation, decision, or action that is focused upon the interest of specific people, or a discrete and identifiable class of people.” It does not refer to “...consideration or adoption of broad policy options directed to the interests of a large and diverse group of people.” [5 C.F.R. § 2640.103(a)(1)]. A particular matter of specific party means a particular matter that is focused on the interests of a specific party [5 C.F.R. § 2640.102(m)].

The activity of the Augmented CAAC for RDX will qualify as a *particular matter involving specific parties* because the resulting advice will be part of a deliberation, and under certain circumstances the advice could involve the interests of a specific party facing regulatory decisions informed by the IRIS RDX toxicological review that may impact the manufacture and distribution of RDX containing products, and the release or disposal of RDX containing waste.

- (ii) Will there be personal and substantial participation on the part of the panel members? Participating personally means direct participation in this review. Participating substantially refers to involvement that is of significance to the matter under consideration.[5 C.F.R. §2640.103(a)(2)]. For this review, the SAB Staff Office has determined that the *Augmented CAAC for RDX members will be participating personally in the matter*. Augmented committee members will be providing the agency with advice and recommendations through the chartered SAB on the agency’s draft *IRIS Toxicological Review of RDX* and such advice is expected to directly influence the agency’s final assessment. *Therefore, participation in this review also will be substantial.*
- (iii) Will there be a direct and predictable effect on panel members’ financial interests? A direct effect on a participant’s financial interest exists if “... a close causal link exists between any decision or action to be taken in the matter on the financial interest..... A particular matter does not have a direct effect ... if the chain of causation is attenuated or is contingent upon the occurrence of events that are speculative or that are independent of, and unrelated to, the matter. A particular matter that has an effect on a financial interest only as a consequence of its effects on the general economy is not considered to have a direct effect.” [5 C.F.R. § 2640.103(a)(ii)]. The ethics regulations include an exemption allowing special government employees (SGEs) serving on federal advisory committees to participate in any particular matter of general applicability where the

disqualifying financial interest arises from their non-Federal employment or non-Federal prospective employment, provided that the matter will not have a special or distinct effect on the employee or employer other than as part of a class [5 C.F.R. § 2640.203(g)]. (This exemption does not include the interests of an SGE arising from the ownership of stock in his employer or prospective employer.)

CAAC members and prospective Augmented CAAC members were asked to submit EPA Form 3110-48, a Confidential Financial Disclosure for Special Government Employees, so that the SAB Staff Office could make this determination. *The SAB Staff Office has determined that there will be no direct and predictable effect on the financial interests of Augmented CAAC for RDX members from their participation on the augmented committee.*

4. How regulations concerning “appearance of a loss of impartiality” pursuant to 5 C.F.R. § 2635.502. apply to members of the Panel.

The Code of Federal Regulations at 5 C.F.R. § 2635.502(a) states that: “Where an employee knows that a *particular matter involving specific parties* is likely to have a **direct and predictable** effect on the financial interest of a member of his household, or knows that a person with whom he has a covered relationship is or represents a party to such matter, and where the person determines that the circumstances would cause a **reasonable person** with knowledge of the relevant facts to question his impartiality in the matter, the employee should not participate in the matter unless he has informed the agency designee of the appearance problem and has received authorization from the agency designee.”

Further, § 2635.502(a)(2) states that, “An employee who is concerned that circumstances other than those specifically described in this section would raise a question regarding his impartiality should use the process described in this section to determine whether he should or should not participate in a particular matter.”

As noted above, the RDX toxicological review can be considered as a particular matter involving specific parties. Prospective augmented committee members were evaluated against the 5 C.F.R. 2635(a)(2) general requirements for considering an appearance of a loss of impartiality. This evaluation included information provided on the EPA Form 3110-48 confidential financial disclosure forms.

For prospective advisory augmented committee members who hold grants, cooperative agreements or contracts or are involved with organizations that can be considered specific parties, the “reasonable person” criterion is met in the following manner:

- i) Those who are or have previously been employed by the regulated community were considered to meet this criterion.
- ii) Those who have a pending grant, cooperative agreement, or contract whose funds could be directly received from organizations that could be considered specific parties to conduct scientific work related to the potential human health effects of RDX were considered to meet the criterion.

5. Other considerations that might affect the objectivity of members of the Panel.

Members of SAB panels must be scientific and technical experts who are objective and open-minded, able to engage in deliberative discussions with scientists who may have disparate perspectives. To evaluate candidates, the SAB Staff Office considers information provided by candidates (including on the EPA Form 3110-48), and information independently gathered by SAB staff.

As part of a determination that committee members are objective and open-minded on the topic of the review, and consistent with the agency's Peer Review Policy, the SAB Staff Office considers previous involvement in the matter before the augmented committee. This evaluation includes responses provided by candidates to the following supplemental questions:

- (a) Do you know of any reason that you might be unable to provide impartial advice on the matter to come before the panel/committee/subcommittee or any reason that your impartiality in the matter might be questioned?
- (b) Have you had any current or previous involvement with the review document(s) under consideration including authorship, collaboration with the authors, or previous peer review functions? If so, please identify and describe that involvement.
- (c) Have you served on previous advisory panels, committees or subcommittees that have addressed the topic under consideration? If so, please identify those activities.
- (d) Have you made any public statements (written or oral) on the issue that would indicate to an observer that you have taken a position on the issue under consideration? If so, please identify those statements.

The SAB Staff Office has determined that there is no reason to believe that the members selected for the Augmented CAAC for RDX would not be objective and open-minded and able to engage in deliberative discussions with scientists who may have disparate points of view on the matter before the augmented committee.

6. How individuals were selected for the augmented committee.

On July 22, 2016, the SAB Staff Office posted a list of 50 candidates for the Augmented CAAC, identified based on their expertise and willingness to be considered for the augmented committee. This list was accompanied by a notice inviting public comments on the list of candidates, to be submitted by August 12, 2016. The SAB Staff Office has not received any comments from the public on this list of candidates.

The SAB Staff Office Director makes the final decision about who serves on the augmented committee based on all of the relevant information, including a review of each candidate's confidential financial disclosure form (EPA Form 3110-48), the responses to the questions above, and information independently gathered by SAB Staff.

For the SAB Staff Office, a balanced committee or panel is characterized by candidates who possess the necessary domains of scientific knowledge, relevant perspectives (which, among other factors, can be influenced by work history and affiliation), and the collective breadth of experience to adequately address the general charge. Specific criteria to be used in evaluating an

individual panel member include: (a) scientific and/or technical expertise, knowledge, and experience; (b) availability and willingness to serve; (c) absence of financial conflicts of interest; (d) absence of an appearance of a loss of impartiality pursuant to 5 C.F.R. § 2635.502; (e) skills working on advisory committees and panels (including objectivity and open-mindedness); and (f) for the committee as a whole, diversity of scientific expertise and viewpoints.

On the basis of the above-specified criteria, the members of the CAAC Augmented for the RDX Review are as follows:

CAAC Augmented for the RDX Review

Dr. Kenneth Ramos, University of Arizona, **CHAIR**
Dr. Hugh Barton, Pfizer, Inc.
Dr. Maarten Bosland, University of Illinois at Chicago
Dr. Mary Boudreau, U.S. Food and Drug Administration
Dr. James Bruckner, University of Georgia
Dr. George Cobb, Baylor University
Dr. David Eastmond, University of California at Riverside
Dr. Joanne English, NSF International
Dr. Alan Hoberman, Charles River Laboratories, Inc.
Dr. Jacqueline Hughes-Oliver, North Carolina State University
Dr. James Klaunig, Indiana University
Dr. Susan Laffan, GlaxoSmithKline, Inc.
Dr. Lawrence Lash, Wayne State University
Dr. Stephen Lasley, University of Illinois at Chicago
Dr. Melanie Marty, University of California at Davis
Dr. Marvin Meistrich, University of Texas
Dr. Diane Miller, Center for Disease Control and Prevention
Dr. Marilyn Morris, State University of New York at Buffalo
Dr. Victoria Persky, University of Illinois at Chicago
Dr. Issac Pessah, University of California at Davis
Dr. Kenneth Portier, American Cancer Society
Dr. Samba Reddy, Texas A & M University
Dr. Stephen M. Roberts, University of Florida
Dr. Thomas Rosol, Ohio State University
Dr. Alan Stern, New Jersey Department of Environmental Protection
Dr. Robert Turesky, University of Minnesota

Concurred,

_____/s/
Christopher S. Zarba
Director and Deputy Ethics Official
EPA Science Advisory Board Staff Office (1400R)

10/5/2016
Date

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). (2012). Toxicological profile for RDX. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.